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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/921,380	08/02/2001	Charles Mark Ensor	PHOE-0061	7237

7590 08/30/2004

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EXAMINER

PATTERSON, CHARLES L JR

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 08/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/921,380

Applicant(s)

ENSOR ET AL.

Examiner

Charles L. Patterson, Jr.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 15 June 2004 and 04 August 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-12, 21-25, 31-37 and 39-43 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-12, 21-25, 31-37 and 39-43 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_.

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A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 8/4/04 has been entered.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12, 21-25, 31-37 and 39-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is enabling for the results shown in Table 1, namely recombinantly produced *Candida utilis* uricase coupled to PEG 5 and PEG 20 at a PEG Number of 19. There are general recitations in the specification of other molecular PEGs and other sources of uricase being used but the only data shown is that in Table 1. One of ordinary skill in the art would believe applicants' data shown in Table 1 but would not believe these other speculative results in the specification.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-12, 21-25, 31-37 and 39-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Williams, et al. (40). The instant reference teaches in at least column 1, lines 17-23 that when polyethylene glycol (PEG) is conjugated to uricase, the circulating lifetimes are prolonged and the immunogenicity is reduced. The use to reduce uric acid levels is taught at least in column 1, line 34-58. Example 4 teaches the uricase from *Candida utilis* conjugated with 30 kDa polyethylene glycol (PEG) with retention of activity. As pointed out by applicants in the reply filed 2/11/03 and as stated on page 11, lines 22-23, "the particular linking groups do not appear to influence the circulating half-life of the PEG-uricase or its specific enzyme activity" and therefor different linking groups would be obvious. Figure 1A shows that the specific activity of the 30 kDa PEG-conjugated uricase increases from 100% with no PEG conjugated to about 118% with 7 strands of PEG coupled per uricase subunit. Fig. 1B shows the specific activity increasing from 100% to about 118% as the mass of PEG coupled per subunit is increased. Figure 2A and 2B show a similar phenomenon with porcine uricase. Figure 3A and 3B shows that when pig-baboon chimeric uricase is coupled to 10 kDa, 19 kDa and 30 kDa PEG, the activity stays above 80% up to 10 strands or 300 kDa of PEG coupled. Figure 4A shows that *A. flavus* has essentially 100% activity up to 7 strands of 200 kDa of 30 kDa PEG coupled.

It would have obvious to one of ordinary skill in the art to couple 12-30 kDa PEG to uricase with the expectation that the circulating lifetimes would be increased and the immunogenicity would be reduced without appreciab-

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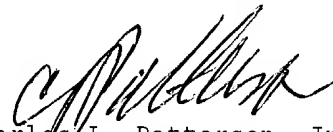
ly reducing activity in view of the instant reference. The additional requirements of the claims such as the identity of the linking groups and the particular uricase used would have been obvious, absent a convincing showing to the contrary. What applicants have actually shown in the specification is that when *Candida utilis* uricase was recombinantly produced in *E. coli*, the specific activity when 19 molecules of 20 kDa PEG was coupled to one molecule of uricase was 75.0% of the native, non-coupled uricase and the circulating half-life was increased (Table 1). This would have been obvious from the teachings of the instant reference which shows that the activity of *Candida* uricase increased up to 7 strands or 200 kDa of 30 kDa PEG added per molecule with no results shown above this. This would indicate to one of ordinary skill in the art that higher amounts of PEG added would also have a high activity. The results with the other three uricases outlined *supra* would indicate to one of ordinary skill in the art that if PEG of 12-30 kDa were added to uricase at a PEG number of 19, a very high percentage of activity would remain with the half-life increasing. There would be at least a reasonable expectation of success.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose telephone number is 571-272-0936. The examiner can normally be reached on Monday - Friday from 7:30 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Charles L. Patterson, Jr.  
Primary Examiner  
Art Unit 1652

Patterson  
August 25, 2004